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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61B 5/04, 17/36, A61F 2/00, 7/00

A1

(11) International Publication Number: WO 98/30144

(43) International Publication Date: 16 July 1998 (16.07.98)

(21) International Application Number: PCT/IL97/00307

(22) International Filing Date: 15 September 1997 (15.09.97)

(30) Priority Data:
PCT/IL97/00011 8 January 1997 (08.01.97) WO
*(34) Countries for which the regional or international application was filed:* IL et al.

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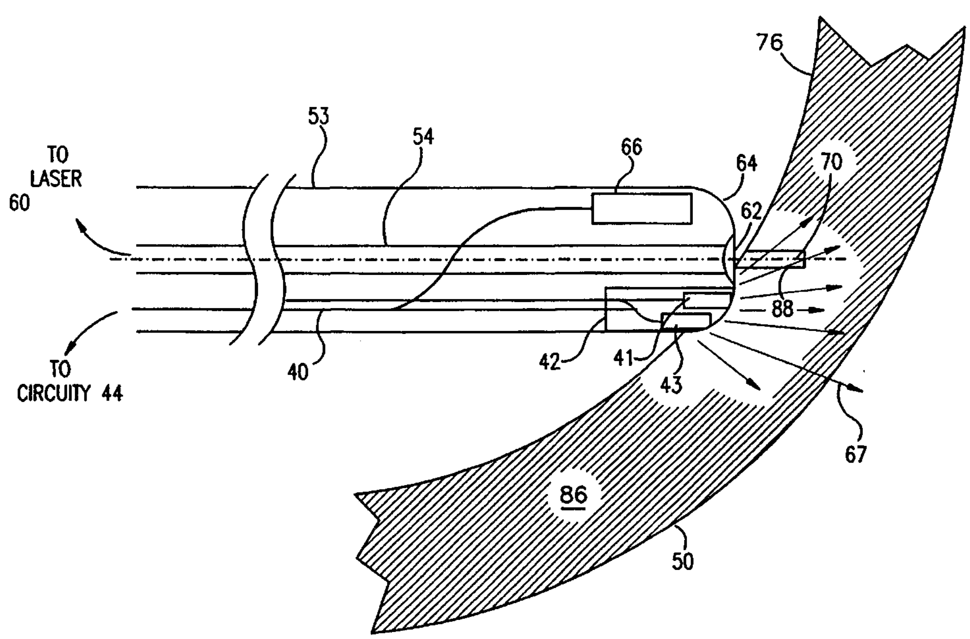
(81) Designated States: AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

**Published**
*With international search report.*

# (54) Title: MONITORING OF MYOCARDIAL REVASCULARIZATION




**(57) Abstract**

This invention is an apparatus for PMR treatment, including an elongate probe (52) having a distal end (64) for engaging heart tissue (86) of a subject, and a revascularization device (60) which imparts energy to the heart tissue (86) for generating perfusion enhancing channels therein. A sensor (42) provides an indication responsive to the treatment, preferably by receiving signals generated by the body of the subject.

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# MONITORING OF MYOCARDIAL REVASCULARIZATION

## RELATED APPLICATION

This application is a continuation-in-part of PCT patent application no. PCT/IL97/00011, filed January 8, 1997, which is incorporated herein by reference.

## FIELD OF THE INVENTION

The present invention relates generally to methods and devices for cardiac surgery, and specifically to methods and apparatus for myocardial revascularization.

## BACKGROUND OF THE INVENTION

Myocardial revascularization is a technique, known in the art, for creating channels in ischemic heart tissue to improve the blood supply to ischemic myocardium. It may be performed by various techniques, the best-known of which is laser myocardial revascularization, which employs laser radiation for generating such channels.

In transmyocardial revascularization (TMR), as is known in the art, a computer-controlled laser is used to drill penetrating holes about 1 mm in diameter in the myocardium by delivering laser energy to the epicardium through an incision in the chest and the pericardium. Blood at the outer, epicardial openings of the channels typically clots after a few minutes, but the inner portions of the channels, communicating with the ventricle, remain patent. It is hypothesized that during systole, blood flows through these channels into naturally-existing myocardial sinusoids, supplementing the impaired arterial blood supply.

According to another hypothesis, the local injury caused to the myocardium by various forms of energy (e.g., laser radiation, as described above, or alternatively, RF radiation, or ultrasonic or mechanical energy) stimulates local angiogenesis, eventually supplementing the impaired arterial blood supply. Although there are no conclusive answers at present regarding the underlying mechanism, there is clinical evidence of the treatment's therapeutic efficacy.

U.S. patent 5,389,096, to Aita, et al., which is incorporated herein by reference, describes methods and apparatus for percutaneous myocardial revascularization (PMR). A deflectable, elongated lasing apparatus is guided to an area within the patient's heart, and the distal end of the apparatus is directed to an area of interest in the inner wall of the heart. The wall is irradiated with laser energy to form channels therein, preferably without perforating the epicardium. Alternatively, PMR may be carried out by applying other energy forms, as described above, from inside the art.

In TMR, as is known in the art, the channels are created through the myocardium from the outside in, and the transient blood stream ensuing upon channel completion constitutes an intrinsic indication of successful drilling. In PMR, however, the channel is generated from inside the heart chamber and, preferably, does not penetrate the myocardium. Consequently there is no direct indication of successful generation of the channel.

A PMR procedure, whether employing laser energy or any other suitable energy form, may fail due to a multiplicity of reasons. For example, referring specifically to laser PMR, the catheter inserted into the heart may be incorrectly oriented, so that the energy does not impact and penetrate the endocardium, or does not penetrate to a significant depth. Alternatively, the distal end of the catheter may be obstructed, for example, by a thrombus and/or ablated tissue residues. Because systems for PMR known in the art do not give any indication of whether the energy pulse has successfully generated a channel in the myocardium, it is difficult or impossible for an interventional cardiologist to detect and correct such a failure during the procedure.

## SUMMARY OF THE INVENTION

It is an object of some aspects of the present invention to provide a reliable indication as to whether an energy pulse locally imparted to the heart has successfully produced a channel in the myocardium.

It is a further object of some aspects of the present invention to provide methods and apparatus for monitored PMR.

In the context of the present patent application and in the claims, the term "PMR" is taken to refer to any and all techniques of percutaneous myocardial revascularization treatment, including laser, RF, ultrasound and mechanical methods, but not limited thereto. Accordingly, while preferred embodiments of the present invention are described herein largely in terms of creating channels in the myocardium using laser irradiation, those skilled in the art will understand that the principles of the present invention are similarly applicable to other PMR techniques.

Some aspects of the present invention are based on the finding by the inventors that when an energy pulse is incident on the myocardium in such a manner as to create a channel therein, it causes detectable variations in the heart's electrical activity, both local and global. In particular, the applicants have observed such variations when a laser beam creates a channel in the myocardium.

The local variation is expressed in the form of an elevated ST segment in the locally-measured electrogram. The elevated ST is characteristic of injuries to the heart, and is observed to last for at least several minutes after generating the channel. It is a distinctly local effect, and is not observed outside a diameter of several millimeters (typically 3 mm) from the point at which the channel is generated.

The global variation is observed in the form of disturbance of the heart's sinus rhythm, typically in one or more ventricular premature beats (VPB's) immediately following the laser pulse. The VPB's are observed both in electrogram signals recorded within the heart chamber and in ECG signals recorded on the body surface.

It is still another object of some aspects of the present invention to provide indication that the channels have been generated in accordance with predetermined dimensions, location and orientation. These aspects of the invention are based primarily on the ability of ultrasonic

waves to resolve zones of differing tissue characteristics, in particular density, thus imaging the channels' dimensions and direction.

Other aspects of the present invention use real-time sensing technologies, particularly based on optical sensing, for detecting local changes in blood perfusion. By comparing pre- and post-PMR optical signals, enhanced blood perfusion of ischemic zones, due to successful channel generation, may be observed.

Some preferred embodiments of the present invention are based on a PMR catheter as described in PCT patent application no. PCT/IL97/00011, filed January 14, 1997, which is assigned to the assignee of the present patent application, and whose disclosure is incorporated herein by reference. The catheter comprises a waveguide, for conveying energy to the endocardium, preferably laser energy, and has at least one sensor at its distal tip. The sensor may comprise one or more electrophysiological sensing electrodes, position sensors, ultrasound transducers, or other sensors known in the art.

In some of these preferred embodiments, the sensor comprises an electrode, which receives electrical signals from the heart indicative of the efficacy of local PMR treatment, i.e., whether an energy pulse or series of pulses has actually succeeded in generating a channel of substantial depth in the myocardium. The catheter is coupled to signal processing circuitry, which processes the signals received by the electrode and provides an indication to a user of the catheter, typically an interventional cardiologist, as to whether the channel has been generated. The indication is typically based on elevation of the ST segment and/or VPB's in the local electrogram during at least several minutes after the channel has been generated. Failure to sense such a change after one or several energy pulses is taken to be an indication of an error or malfunction, requiring the cardiologist's intervention. Preferably, the catheter is held in place at a candidate site for a period both before and after channel generation, long enough to gather pre- and post-PMR electrograms, which are compared to ascertain the efficacy of the local treatment.

Preferably, the elevated ST effect, which is of a highly localized nature and significantly long duration, also provides an indication to the user during subsequent PMR channel generation as to whether a channel preexists in a new candidate area.

In some of these preferred embodiments, the electrode is used for gating the energy source, as described in PCT patent application no. PCT/IL97/00011, mentioned above, as well as sensing signals indicative of successful channel generation.

In some preferred embodiments of the present invention, ECG is measured during the PMR procedure by means of skin electrodes. Disturbances of the normal sinus rhythm, particularly ventricular premature beats (VPB's), are sensed as an indication that an energy pulse has successfully generated a channel in the myocardium. Absence of such disturbance is, similarly, taken to indicate error or malfunction.

In other preferred embodiments of the present invention, the sensor at the distal end of the catheter comprises an ultrasonic transducer. The transducer generates signals responsive to

the changes induced in the myocardial tissue by the channel generation operation. The signals are used to detect successful generation of the channel, alone or in conjunction with internal or external ECG readings.

Preferably, the ultrasonic signals are further used to monitor the depth and/or direction of the channel generated by the radiation.

In further preferred embodiments of the present invention, the sensor at the distal end of the catheter comprises a blood flow sensor, preferably an optical sensor or, alternatively, an ultrasonic sensor, which generates signals responsive to local microcirculation blood flow. The signals are used to detect successful reperfusion at the treated site.

In alternative preferred embodiments of the present invention, the sensor at the distal end of the catheter comprises an optical sensor, which receives light emitted by endocardial tissue. Light is transmitted from a radiation source, optionally via the waveguide in the catheter, as described above, to the myocardial tissue. The radiation is tuned to be absorbed by substances in the tissue related to local blood perfusion and stimulate them to fluoresce (i.e., autofluorescence). The emitted autofluorescent radiation is received by the optical imaging sensor and is measured to detect successful channel generation. For example, the sensor may be used to detect local NADH levels, which are correlated with ischemia, as described in a series of publications, including Kedem et al., Q.J. Exp. Physiol. 66:501-514, 1981; Furman et al., Cardiovasc. Res. 10:606-612, 1985; and Duboc et al., Lancet, Aug. 30 1986, p. 522, which are incorporated herein by reference.

Alternatively, fluorescing contrast agents, known in the art, such as fluorescein or indocyanine green (ICG), may be injected into the blood stream to facilitate photo-detection of local blood perfusion by angiography. Such methods are described, for example, in U.S. Patent 5,566,673, to Shiono, and in an article by May in Biophotonics International, May/June 1995, pp. 44-50, which are incorporated herein by reference.

Although preferred embodiments are described herein with reference to certain types of PMR catheters, in particular those described in the above-mentioned PCT patent application no. PCT/IL/00011, it will be appreciated that the principles of the present invention may similarly be applied using other types of catheters and apparatus, as are known in the art. In particular, as noted above, the catheter may comprise a device for imparting to the heart energy forms other than laser radiation, for example, RF, ultrasonic or mechanical energy.

There is thus provided, in accordance with a preferred embodiment of the present invention, apparatus for PMR treatment, including:

an elongate probe having a distal end for engaging heart tissue of a subject, and including a revascularization device, which imparts energy to the heart tissue for generating perfusion-enhancing channels therein; and

a sensor, which provides an indication responsive to the treatment.

Preferably, the sensor receives signals generated by the body of the subject responsive to the treatment.

Further preferably, the sensor includes an electrode, which is positioned on the probe adjacent the distal end thereof.

Alternatively or additionally, the electrode is placed on the subject's body independently of the probe.

In preferred embodiments, the sensor includes a transducer, preferably an ultrasonic transducer, which generates signals indicative of the treatment.

Alternatively or additionally, the sensor includes a blood flow sensor, which generates signals responsive to microcirculation.

Preferably, the transducer is positioned on the probe adjacent the distal end thereof.

In another preferred embodiment, the sensor includes an optical sensor, and the apparatus preferably includes a waveguide, which transmits fluorescence-stimulating radiation to the myocardial tissue, wherein the sensor receives fluorescence emitted from the tissue and generates signals indicative of the treatment.

Preferably the apparatus includes signal processing circuitry, which is coupled to the sensor and analyzes the signals to provide an indication of the efficacy of the treatment. Preferably, the circuitry detects an elevated ST segment or, alternatively or additionally, an arrhythmia. Preferably, the arrhythmia detected by the circuitry includes at least one VPB.

Alternatively or additionally, the circuitry detects a change in tissue characteristics adjacent to the distal end of the probe. Preferably, the change includes a change in tissue density, or, alternatively or additionally, an increase in blood perfusion adjacent to the distal end of the probe.

Preferably, the revascularization device applies laser radiation to the heart tissue.

Alternatively, the revascularization device applies RF energy, high-intensity ultrasonic radiation, and/or mechanical energy to the heart tissue.

There is also provided, in accordance with a preferred embodiment of the present invention, a method for monitored PMR treatment of the heart of a subject, including:

bringing a probe, including a revascularization device for imparting energy to the heart, into engagement with heart tissue of a subject;

imparting energy to the heart tissue using the device so as to generate perfusion-enhancing channels therein; and

receiving a signal from the body of the subject responsive to the treatment.

Preferably, receiving the signal includes receiving a signal generated by the body of the subject indicative of successful performance of the treatment.

Further preferably, sensing the signal includes sensing an electrical signal inside the heart of the subject, or,

alternatively or additionally, on a surface of the body of the subject.

In a preferred embodiment, receiving the signal includes receiving energy reflected from the heart tissue, preferably ultrasonic energy reflected from a designated channel location within the heart.

In another preferred embodiment, receiving energy includes receiving fluorescence radiation emitted from the heart tissue, preferably autofluorescent radiation or, alternatively, from an agent administered into the subject's blood stream.

In still another preferred embodiment, receiving the signal includes receiving signals responsive to microcirculation blood flow rate adjacent a designated channel location within the heart.

Preferably, the above method includes processing the signals to provide an indication of the efficacy of the treatment, most preferably by detecting an elevated ST segment, or alternatively or additionally, by detecting an arrhythmia. Preferably, detecting the arrhythmia includes detecting a VPB.

In a preferred embodiment, processing the signals includes detecting changes in tissue characteristics in the channel area, preferably detecting changes in tissue density.

Alternatively, processing the signals includes detecting changes in blood perfusion in the tissue, preferably, detecting an enhancement of the perfusion.

Preferably, imparting energy to the heart includes imparting laser radiation.

Alternatively, imparting energy to the heart includes imparting RF radiation, high-intensity ultrasonic radiation, or mechanical energy.

The present invention will be more fully understood from the following detailed description of the preferred embodiments thereof, taken together with the drawings in which:

## BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1A is a schematic illustration showing electrical signals received from the body of a subject before, during and after PMR laser firing;

Fig. 1B is a schematic illustration showing the signals of Fig. 1A on an expanded time scale;

Fig. 2A is a schematic illustration of a catheter system for use in PMR, in accordance with a preferred embodiment of the present invention;

Fig. 2B is a schematic illustration showing details of the distal end of the catheter of Fig. 2A, in accordance with a preferred embodiment of the present invention;

Fig. 3A is a schematic, sectional illustration of a human heart, into which the catheter of Figs. 2A and 2B is inserted for performing a PMR procedure therein, in accordance with a preferred embodiment of the present invention;

Fig. 3B is a schematic, sectional detail illustration showing a channel drilled in the tissue of the heart of Fig. 3A, in accordance with a preferred embodiment of the present invention;

Fig. 4 is a schematic illustration showing details of the distal end of a catheter for PMR, in accordance with an alternative preferred embodiment of the present invention;

Fig. 5 is a schematic illustration of a human body and heart, into which the catheter of Figs. 2A and 2B is inserted to perform a PMR procedure therein, in accordance with another preferred embodiment of the present invention;

Fig. 6 is a flowchart illustrating a method of monitored PMR, in accordance with a preferred embodiment of the present invention;

Fig. 7A is a schematic illustration showing details of the distal end of a catheter for PMR, in accordance with an alternative preferred embodiment of the present invention; and

Fig. 7B is a schematic illustration showing details of the distal end of a catheter for PMR, in accordance with yet another preferred embodiment of the present invention.

## DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Reference is now made to Figs. 1A and 1B, which are graphs schematically depicting signals received from the body of a dog undergoing an experimental PMR treatment, using a laboratory system similar to that which is shown schematically in Fig. 2A below and described with reference thereto.

The traces in Figs. 1A and 1B represent ECG signals 10 received from body surface electrodes, intracardiac electrogram signals 20 received from an electrode on a PMR catheter, as described below, and a trigger pulse 30 applied to a laser source used in performing the PMR treatment. Fig. 1B shows a portion 11 of the traces of Fig. 1A on an expanded time scale.

As shown in the figures, it has been found that injury to the heart tissue due to PMR drilling induces specific local and global variations in the electrical activity of the heart. The local variation manifests itself in the form of an elevated ST segment 24 in locally-measured electrogram 20, which was found to last for several minutes after PMR drilling.

The global variation is observed as a disturbance of the heart's normal sinus rhythm, typically in the form of one or more ventricular premature beats (VPB's) 14 in ECG trace 10 and electrogram trace 20, immediately following the laser pulse.

In the course of experiments performed on 25 dogs, elevated ST segments were observed after at least 60% of the PMR laser pulses and VPB's were observed after at least 95% of the PMR laser pulses administered to the dogs. These variations in the heart's normal electrical activity were found to correlate with successful PMR drilling. The elevated ST segments are considered by the applicants more reliable in this respect, due to the lesser number of false positives encountered. When either the elevated ST segment or VPB's were not observed following a laser pulse, it was found that a channel had not been generated, i.e., no false negatives were encountered.

Reference is now made to Figs. 2A and 2B, which schematically illustrate a system 50 for PMR, including a catheter 52 for insertion into the body of a subject, in accordance with a preferred embodiment of the present invention. Catheter 52 comprises an optical waveguide 54, as is known in the art, for transmitting laser energy from the laser source to the heart tissue. A focusing lens 62 at distal end 64 of catheter 52 focuses the laser radiation from waveguide 54 into heart tissue. Catheter 52 is connected at its proximal end 56 to a console 58, which includes a laser source 60 optically coupled to waveguide 54. The laser is activated to generate PMR channels into the heart tissue. Optionally, console 58 includes an optical radiation source 61, which is used in conjunction with a catheter comprising an optical sensor for measuring local blood perfusion (as shown in detail in Fig. 7B and described with reference thereto).

Preferably, console 58 also includes signal processing circuitry 44, as well as a display 46 and user controls 48. Preferably, intracardiac electrogram trace 10, the skin ECG trace 20 and/or the laser trigger signal 30 are monitored and displayed on display 46 during the PMR treatment. As described above, these traces provide a real-time visual indication to the user of

the catheter, typically an interventional cardiologist, as to whether the channel has been generated.

Additionally or alternatively, the signal processing circuitry analyzes the data and gives the user a “go/no go” indication as to whether the channel has been successfully generated.

Catheter 52 preferably also includes a position sensor 66, fixed in a known position adjacent distal end 64, for use in navigating and positioning the catheter within the heart, as described more fully in PCT patent application no. PCT/IL97/00011, incorporated herein by reference.

As shown in Fig. 2B, catheter 52 includes a sensor unit 42 at its distal end 64. Preferably, sensor unit 42 comprises an electrode 43 for sensing electrical potentials in heart tissue adjacent to distal end 64. Local electrogram signals from electrode 43 are conveyed by wires 40 to circuitry 44. Preferably, these signals are used to monitor the changes in the electrogram signals due to the PMR drilling, as described above, thus indicating successful channel drilling. The electrogram signals may also be used to trigger laser source 60, as disclosed in PCT patent application no. PCT/IL97/00011, mentioned above.

Although catheter system 50 is shown and described with reference to electrode 43, it will be understood that sensor unit 42 may include other sensors and other types of elements. For example, additional electrodes may be placed at or adjacent to distal end 64, either on catheter 52 itself or on a structure fixed to the catheter, as described in PCT patent application no. PCT/IL97/00009, filed January 8, 1997, which is assigned to the assignee of the present patent application, and whose disclosure is incorporated herein by reference.

Fig. 3A is a schematic, sectional illustration showing catheter 52 inserted into heart 70 of a subject, in accordance with a preferred embodiment of the present invention. Catheter 52 is fed percutaneously into the subject's vascular system, for example, through the femoral artery, and is passed through aorta 72 into left ventricle 74 of heart 70. Distal end 64 is positioned against endocardium 76 in a desired position and orientation and drills channels therein, preferably, as described in the above-mentioned PCT patent application no. PCT/IL97/00011.

Fig. 3B is a schematic, sectional illustration showing details of catheter 52 drilling a channel 88 in myocardium 86 of heart 70, in accordance with a preferred embodiment of the present invention. Electrode 43 measures the local electrical signals prior to, during and after the drilling to assess successful drilling, as described above.

Fig. 4 is a schematic illustration showing details of another catheter 53 for use in PMR, in accordance with alternative preferred embodiments of the present invention. Catheter 53 includes waveguide 54, lens 62 and position sensor 66, and is coupled to console 58, substantially as described above with reference to catheter 52. Additionally, sensor unit 42 of catheter 53 includes an ultrasound transducer 41. Preferably, transducer 41 comprises a transducer array, as is known in the art, which emits a beam 67 that may be steered over a range

of angles within an area distal to distal end 64 of catheter 53. Transducer 41 is coupled via wires 40 to signal processing circuitry 44.

Catheter 53 is preferably brought into contact with endocardium 76, as shown in Fig. 4. Preferably, signals received by circuitry 44 from transducer 41 are used to map the designated channel location prior to and after the PMR procedure to determine, by means of comparison, the dimensions, location and orientation of channel 88, thus indicating its successful generation.

Alternatively or additionally, the ultrasonic readings may be used for dynamic monitoring of channel parameters. Preferably, following each pulse or several pulses of the laser source, the transducer signals are used to measure the depth and direction of channel 88 and determine whether the optimal, desired depth has been reached and whether catheter 53 is properly aimed.

In some preferred embodiments of the present invention, transducer 41 and electrode 43 are used in tandem for assessing successful completion of the PMR procedure, by combining data regarding variations in the electrogram signals following PMR drilling with quantitative measurement of dimensional parameters of channel 88.

Although in the embodiments described above, catheters 52 and 53 include various sensors and optical elements in certain preferred combinations and configurations, it will be appreciated that in other preferred embodiments of the present invention, PMR catheters may include some or all of these sensors and elements in other combinations and in the same or other configurations. Such catheters may also include other types of sensors known in the art, for example, temperature or pressure sensors, useful in diagnosing other aspects of cardiac function. They may further include blood flow sensors for measuring the local microcirculation flow rate, or optical sensors for visualizing local blood perfusion by tissue autofluorescence or angiography enhanced by fluorescing contrast agents.

Fig. 5 is a schematic illustration showing the use of skin electrodes 45 placed on a subject's body 71 to record ECG signals therefrom during a PMR procedure, in accordance with a preferred embodiment of the present invention. Preferably, electrodes 45 record the skin ECG signals prior to and for several minutes after laser firing to assess successful drilling, primarily by observing VPB's, as described above with reference to Figs 1A and 1B.

In some preferred embodiments of the present invention, the global changes sensed by skin electrodes 45 may serve as the sole indication of successful drilling.

Alternatively, in other preferred embodiments of the present invention, the global variations monitored in the ECG signals are used in conjunction with local variations in the electrical signals sensed by electrode 43.

Further alternatively or additionally, in some preferred embodiments, the signals measured by electrodes 45 may be used in conjunction with measurements from ultrasonic transducer 41, as described above with reference to Fig. 4.

Fig. 6 is a flow chart that summarizes the key steps in a method for monitored PMR, in accordance with preferred embodiments of the present invention. The method is described

below with reference to catheter 52, shown in Figs. 2A and 2B, but it will be understood that the principles of this method may be applied using other suitable catheters, as described hereinabove.

Prior to beginning PMR, at least one candidate area for the procedure is identified within heart 70, preferably as described in the above-mentioned PCT patent application no. PCT/IL97/00011.

Catheter 52 is then navigated to the candidate area. The position and orientation of distal end 64 of the catheter are preferably ascertained and controlled by receiving signals from position sensor 66, and are compared with a stored map of the heart, although such position and orientation sensing are not a necessary part of the present invention. When the distal end is suitably positioned and oriented, intracardiac electrogram signals are received and stored by console 48. Laser source 60 is fired to drill a channel in the heart tissue, as described above. Following the laser firing, post-PMR readings are taken by electrode 43 and analyzed, preferably by comparing them with the pre-PMR signals, for indication of successful drilling. The position of the channel is marked on the map, and catheter 52 is then repositioned to drill the next channel. This procedure is preferably repeated until channels have been drilled to a desired density over the entire candidate area.

It will be understood that as described above, the method of monitored PMR shown in Fig. 6 may similarly be implemented by monitoring the skin surface ECG or by using ultrasound or other sensing modalities. Similarly, the PMR procedure may be carried out using other methods of PMR, such as RF or mechanical methods, mentioned above, in place of the laser.

Reference is now made to Fig. 7A, which is a schematic illustration showing details of a catheter 90 for use in monitored PMR, in accordance with an alternative preferred embodiment of the present invention. Catheter 90 includes waveguide 54, lens 62 and position sensor 66, and is coupled to console 58, substantially as described above with reference to catheter 52. Additionally, sensor unit 42 of catheter 90 includes a blood flow sensor 92, which senses signals responsive to blood flow within microvasculature 94 in a vicinity of channel 88, generated by the catheter.

Sensor 92 preferably comprises an optical detector, which senses microperfusion and/or tissue oxygenation based on light reflected from the heart tissue. For example, the sensor may be used to detect NADH activity, as described in the above-mentioned articles by Kedem, Furman and Duboc, or to detect the concentration of a contrast agent or fluorescent marker. Alternatively, sensor 92 may comprise an ultrasound transducer. Sensor 92 is coupled via wires 40 to circuitry 44.

When catheter 90 is brought into contact with endocardium 76, sensor 92 receives signals from the vicinity of channel 88. Signals prior to and after the PMR procedure are compared, so as to detect changes in local blood flow in the vicinity. An enhancement of the local blood flow following the procedure, indicated by increased microperfusion and/or tissue oxygenation, is generally a sign of successful channel generation.

Fig. 7B schematically illustrates a catheter 96, similar in design and function to catheter 90 described above, in accordance with another preferred embodiment of the present invention. Sensor unit 42 of catheter 96 includes an optical sensor assembly 102, comprising a waveguide 98, which is connected to radiation source 61 (shown in Fig. 2A) and transmits fluorescence-stimulating radiation to the myocardial tissue through a lens 100. Assembly 102 further comprises a light detector 104, connected via wires 40 to circuitry 44. Detector 104 receives fluorescent radiation emitted from the tissue and generates signals in response thereto. For example, the detector may detect near-IR fluorescence of ICG injected into the patient's bloodstream and conveyed thereby to microvasculature 94, as described in the above-mentioned article by May. Preferably, detector 104 includes an optical filter, as is known in the art, so that the detector receives radiation only in a wavelength band of interest.

When catheter 96 is brought into contact with the endocardium, sensor assembly 102 receives signals in the vicinity of channel 88 prior and after the PMR procedure to determine changes in local perfusion, as explained above. Increased perfusion generally indicates a successful PMR treatment.

It will be appreciated that the principles and methods of the present invention may be applied using catheters and apparatus of other types known in the art, to generate channels 88. These channels may be drilled using a laser source, as described above, or alternatively, using drills of other suitable types known in the art, for example, a high-speed roto-ablator drill head. Alternatively, the channels may be produced using a focused, high-intensity beam of ultrasonic radiation, or by applying RF energy to the tissue. Although in the preferred embodiments described above, catheters 52, 53, 90 and 96 are used to produce channels in the wall of left ventricle 74, it will also be understood that the principles of the present invention may be applied to assess the efficacy of PMR procedures applied to other parts of the heart.

It is believed that other physiological parameters may also be affected by PMR channel generation in the heart. It will therefore be evident to those skilled in the art that the principles of the present invention may be applied using other types of sensors, as appropriate, to provide signals responsive to channel generation.

It will be appreciated that the preferred embodiments described above are cited by way of example, and the full scope of the invention is limited only by the claims.

## CLAIMS

1. Apparatus for PMR treatment, comprising:

an elongate probe having a distal end for engaging heart tissue of a subject, and comprising a revascularization device, which imparts energy to the heart tissue for generating perfusion-enhancing channels therein; and

a sensor, which provides an indication responsive to the treatment.

2. Apparatus according to claim 1, wherein the sensor receives signals generated by the body of the subject responsive to the treatment.

3. Apparatus according to claim 2, wherein the sensor comprises an electrode.

4. Apparatus according to claim 3, wherein the electrode is positioned on the probe adjacent the distal end thereof.

5. Apparatus according to claim 3, wherein the electrode is placed on the subject's body independently of the probe.

6. Apparatus according to claim 1, wherein the sensor comprises a transducer which generates signals indicative of the treatment.

7. Apparatus according to claim 6, wherein the transducer comprises an ultrasonic transducer.

8. Apparatus according to claim 6, wherein the transducer is positioned on the probe adjacent the distal end thereof.

9. Apparatus according to claim 1, wherein the sensor comprises a blood flow sensor, which generates signals responsive to microcirculation.

10. Apparatus according to claim 1, wherein the sensor comprises an optical sensor.

11. Apparatus according to claim 10, and comprising a waveguide, which transmits fluorescence-stimulating radiation to the myocardial tissue, wherein the sensor receives fluorescence emitted from the tissue and generates signals responsive thereto.

12. Apparatus according to any of the preceding claims, and comprising signal processing circuitry, which is coupled to the sensor and analyzes the signals to provide an indication of the efficacy of the treatment.

13. Apparatus according to claim 12, wherein the circuitry detects an elevated ST segment.

14. Apparatus according to claim 12, wherein the circuitry detects an arrhythmia.

15. Apparatus according to claim 14, wherein the arrhythmia detected by the circuitry comprises at least one VPB.

16. Apparatus according to claim 12, wherein the circuitry detects a change in tissue characteristics adjacent to the distal end of the probe.

17. Apparatus according to claim 16, wherein the change in tissue characteristic comprises a change in tissue density.

18. Apparatus according to claim 12, wherein the circuitry detects an increase in blood perfusion adjacent to the distal end of the probe.

19. Apparatus according to any of claims 1-11, wherein the revascularization device applies laser radiation to the heart tissue.

20. Apparatus according to any of claims 1-11, wherein the revascularization device applies RF energy to the heart tissue.

21. Apparatus according to any of claims 1-11, wherein the revascularization device applies high-intensity ultrasonic radiation to the heart tissue.

22. Apparatus according to any of claims 1-11, wherein the revascularization device applies mechanical energy to the heart tissue.

23. A method for monitored PMR treatment of the heart of a subject, comprising:

bringing a probe, including a revascularization device for imparting energy to the heart, into engagement with heart tissue of a subject;

imparting energy to the heart tissue using the device so as to generate perfusion-enhancing channels therein; and

receiving a signal from the body of the subject responsive to the treatment.

24. A method according to claim 23, wherein receiving the signal comprises receiving a signal indicative of successful performance of the treatment.

25. A method according to claim 23, wherein receiving the signal comprises sensing a signal generated by the body of the subject.

26. A method according to claim 25, wherein sensing the signal comprises sensing an electrical signal inside the heart of the subject.

27. A method according to claim 25, wherein sensing the signal comprises sensing an electrical signal on a surface of the body of the subject.

28. A method according to claim 23, wherein receiving the signal comprises receiving energy reflected from the heart tissue.

29. A method according to claim 28, wherein receiving energy comprises receiving ultrasonic energy from a designated channel location within the heart.

30. A method according to claim 28, wherein receiving energy comprises receiving fluorescence radiation emitted from the heart tissue.

31. A method according to claim 30, wherein receiving fluorescence radiation comprises receiving autofluorescent radiation.

32. A method according to claim 30, wherein receiving fluorescence radiation comprises receiving fluorescent radiation from an agent administered into the subject's blood stream.

33. A method according to claim 23, wherein receiving the signal comprises receiving signals responsive to microcirculation blood flow rate adjacent a designated channel location within the heart.

34. A method according to any of claims 23-33, and comprising processing the signals to provide an indication of the efficacy of the treatment.

35. A method according to claim 34, wherein processing the signals comprises detecting an elevated ST segment.

36. A method according to claim 34, wherein processing the signals comprises detecting an arrhythmia.

37. A method according to claim 36, wherein detecting the arrhythmia comprises detecting a VPB.

38. A method according to claim 34, wherein processing the signals comprises detecting a change in a tissue characteristic in the channel area.

39. A method according to claim 38, wherein detecting the change comprises detecting a change in tissue density.

40. A method according to claim 38, wherein detecting the change comprises detecting a change in blood perfusion in the tissue.

41. A method according to claim 40, wherein detecting the change in blood perfusion comprises detecting an enhancement of the perfusion.

42. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting laser radiation.

43. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting RF radiation.

44. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting high-intensity ultrasonic radiation.

45. A method according to any of claims 23-33, wherein imparting energy to the heart comprises imparting mechanical energy.

FIG. 1A

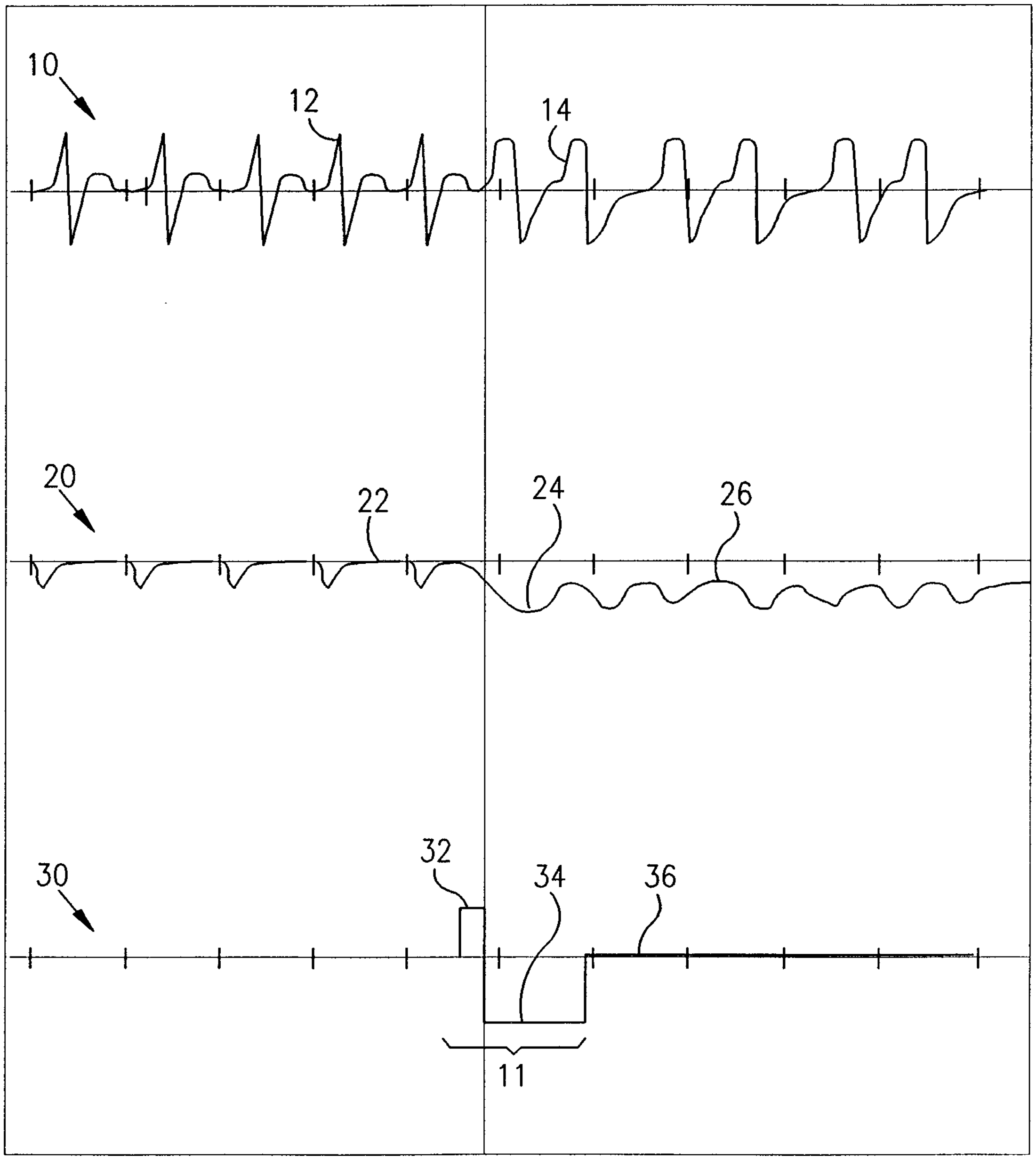
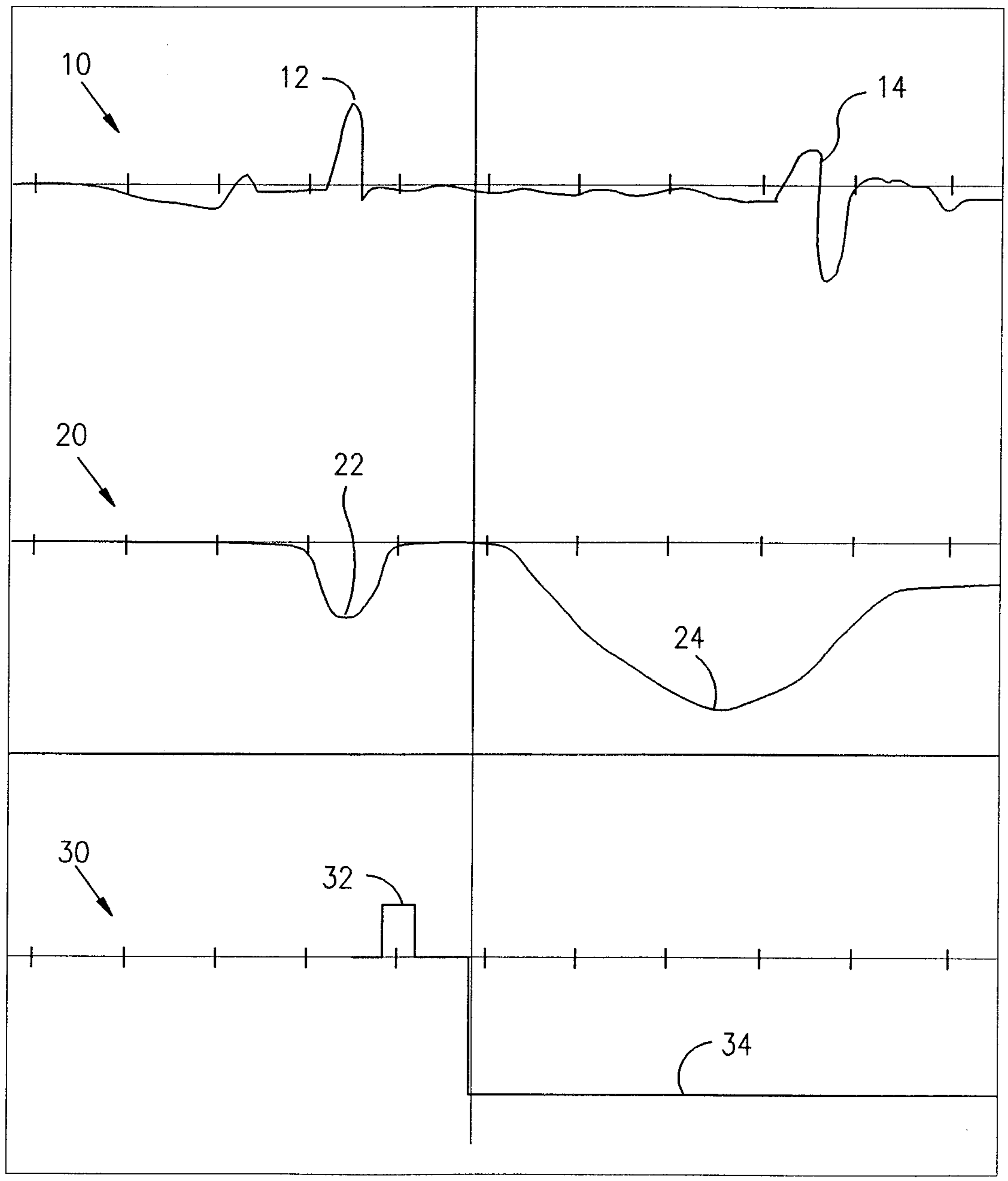


FIG. 1B



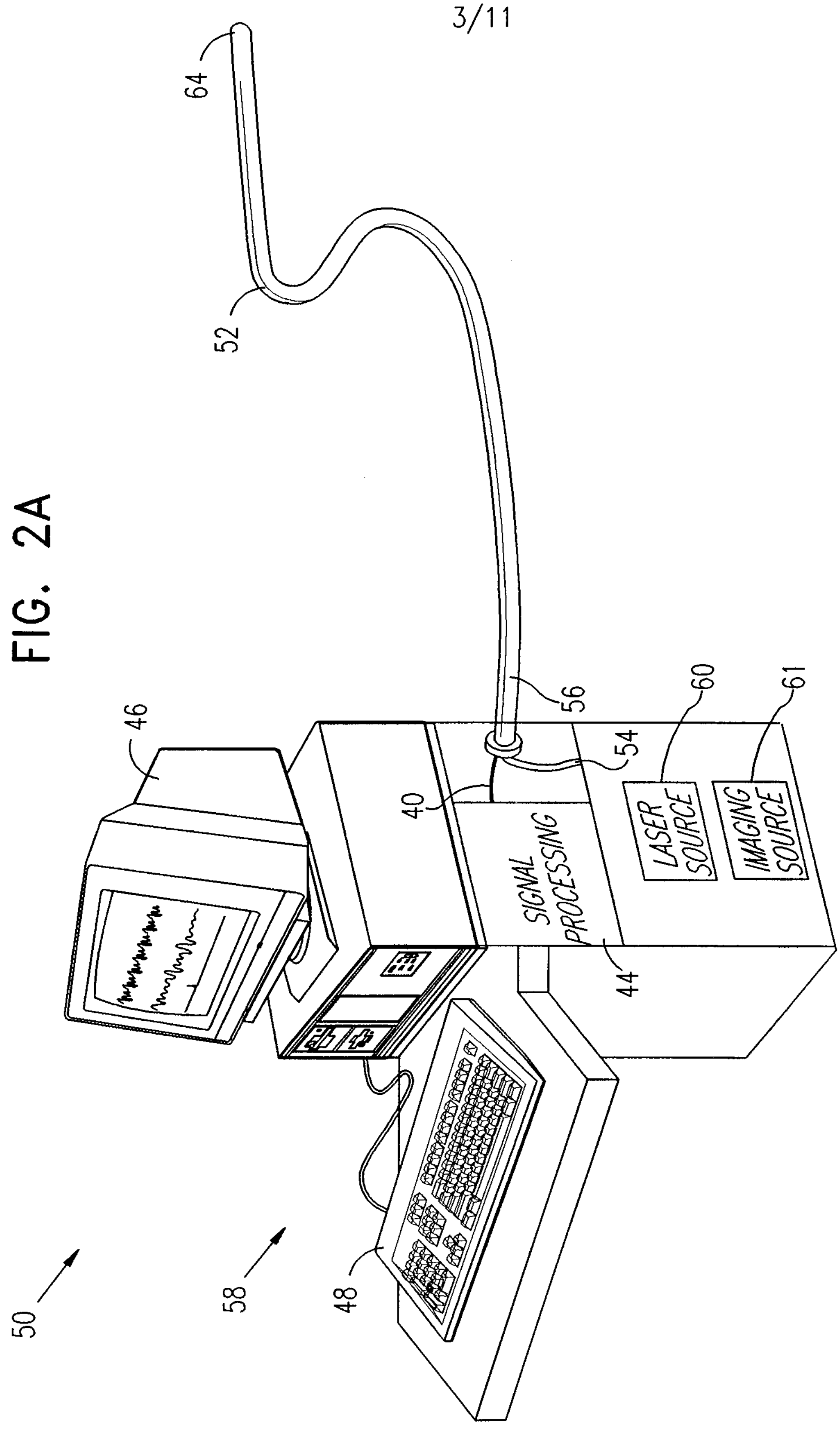

64
52
56
54
40
46
SIGNAL PROCESSING
LASER SOURCE
IMAGING SOURCE
60
61
44
48
58
50

FIG. 2A

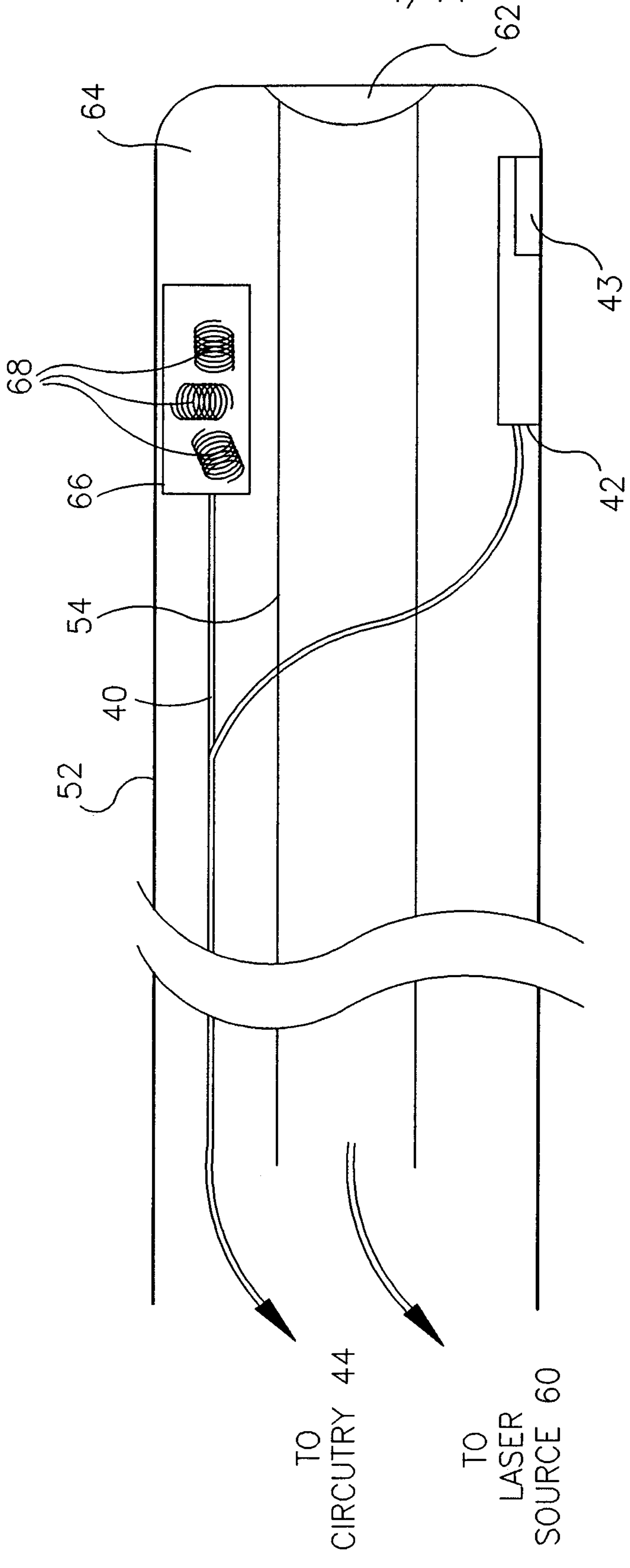



FIG. 2B

FIG. 3A

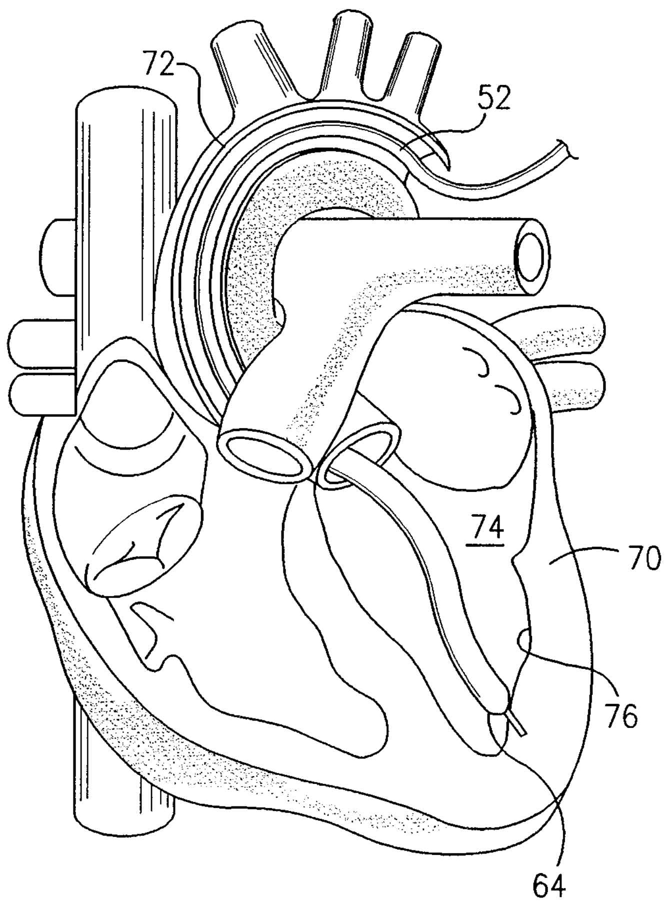
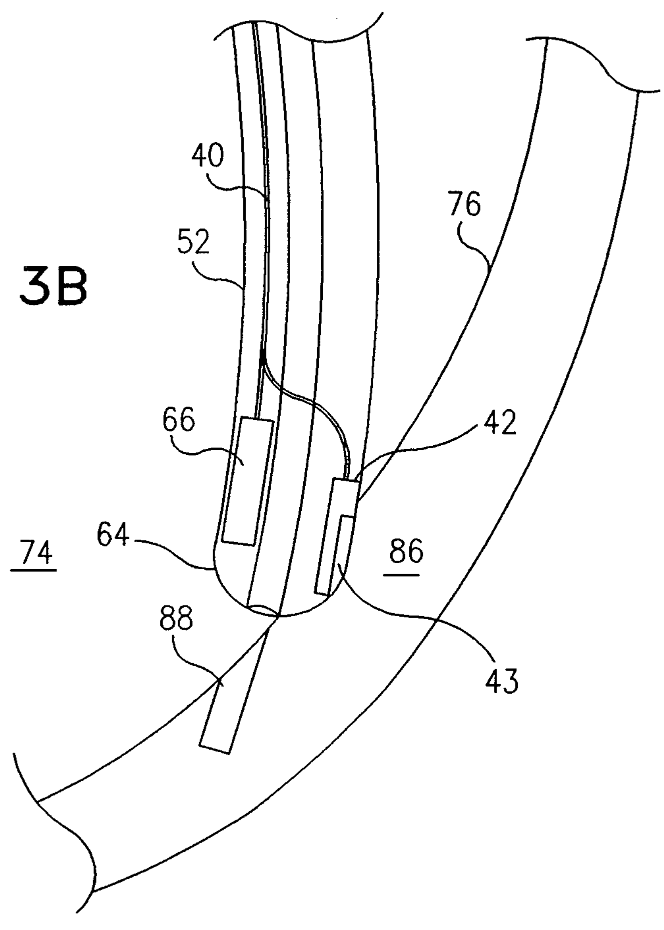
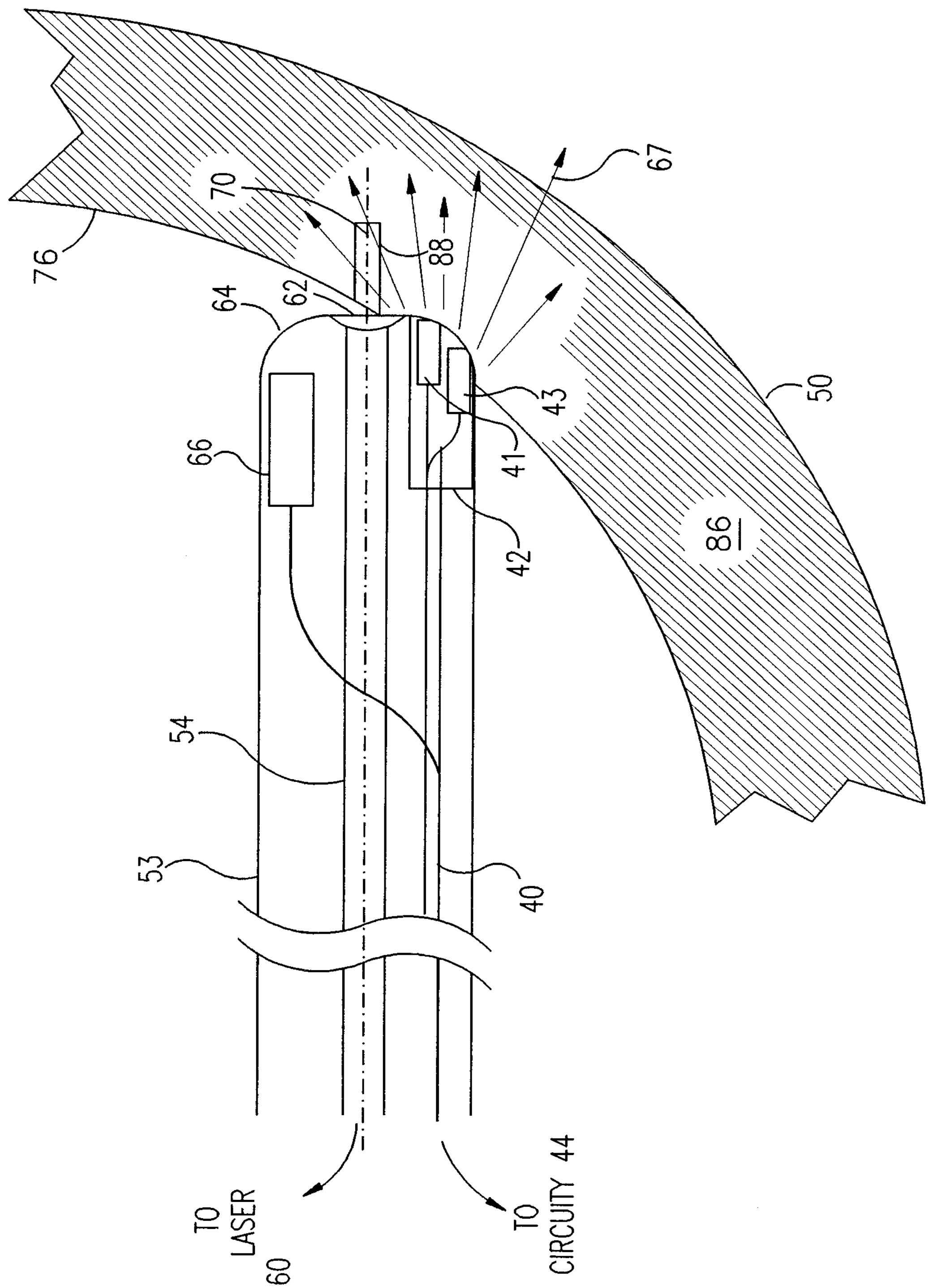


FIG. 3B





70
88
67
76
64
62
66
43
41
50
86
42
54
53
40
TO LASER 60
TO CIRCUITY 44


FIG. 4

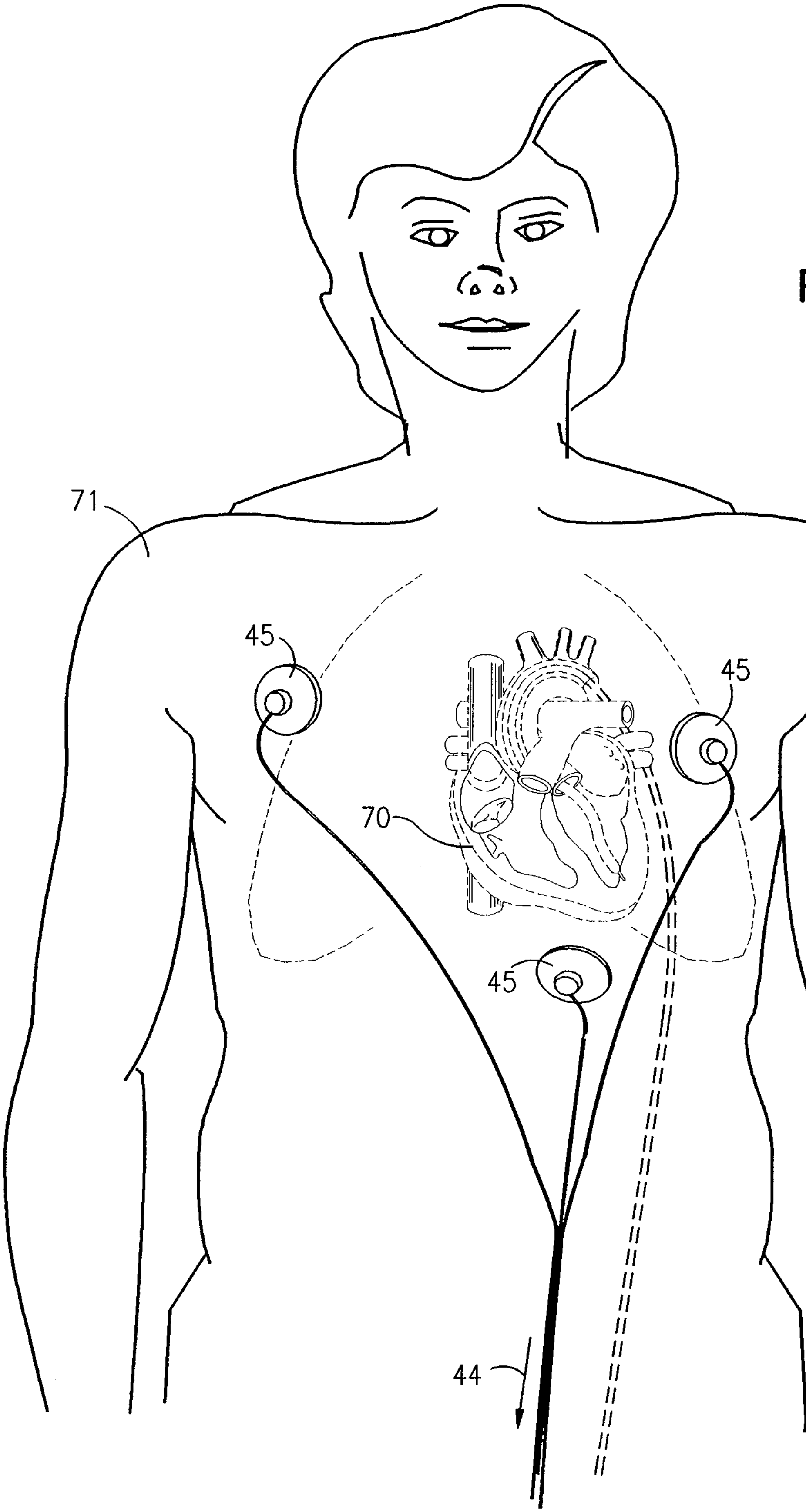



FIG. 5

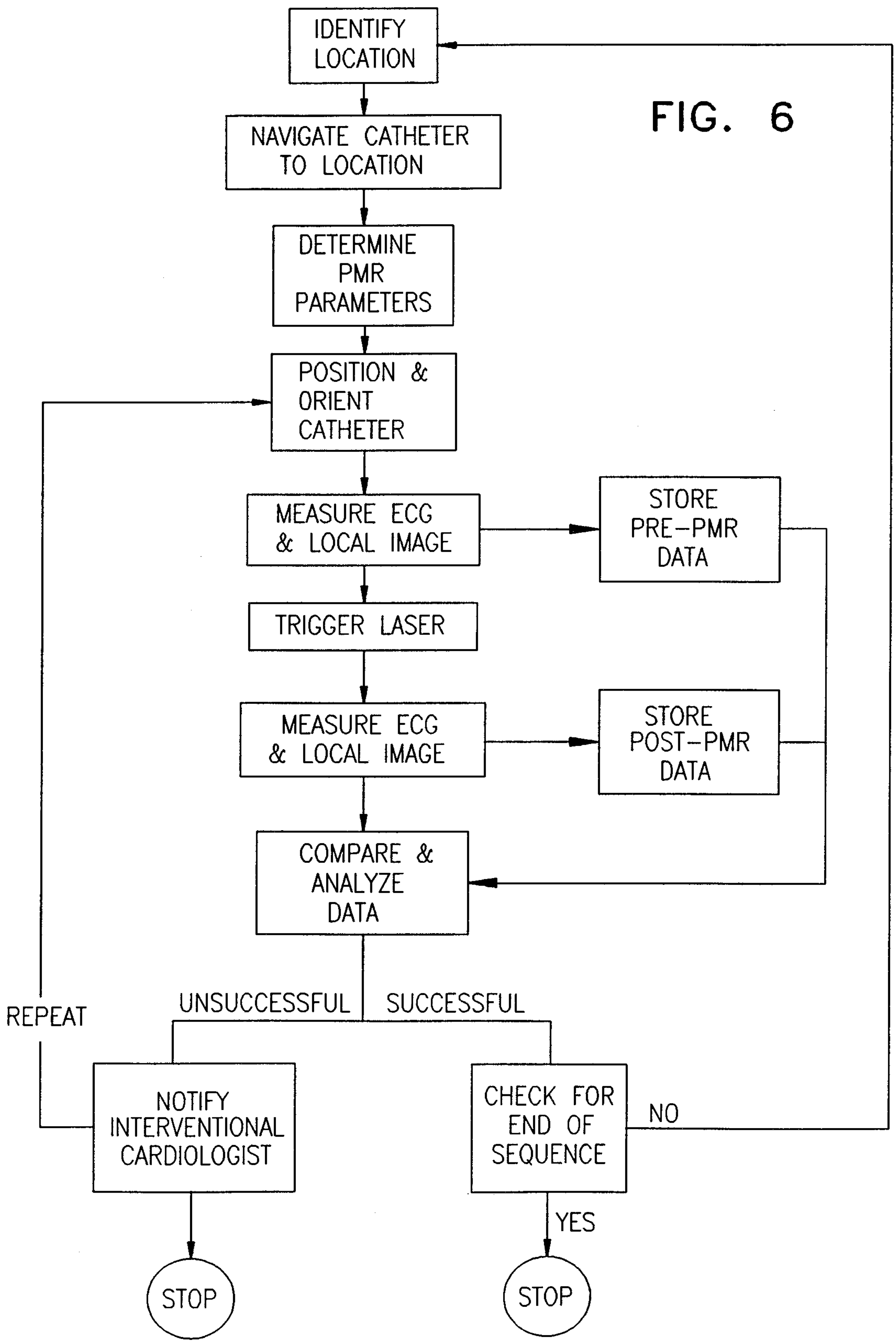

IDENTIFY LOCATION
NAVIGATE CATHETER TO LOCATION
DETERMINE PMR PARAMETERS
POSITION & ORIENT CATHETER
MEASURE ECG & LOCAL IMAGE
STORE PRE-PMR DATA
TRIGGER LASER
MEASURE ECG & LOCAL IMAGE
STORE POST-PMR DATA
COMPARE & ANALYZE DATA
UNSUCCESSFUL
SUCCESSFUL
REPEAT
NOTIFY INTERVENTIONAL CARDIOLOGIST
CHECK FOR END OF SEQUENCE
NO
YES
STOP
STOP

FIG. 6

FIG. 7A

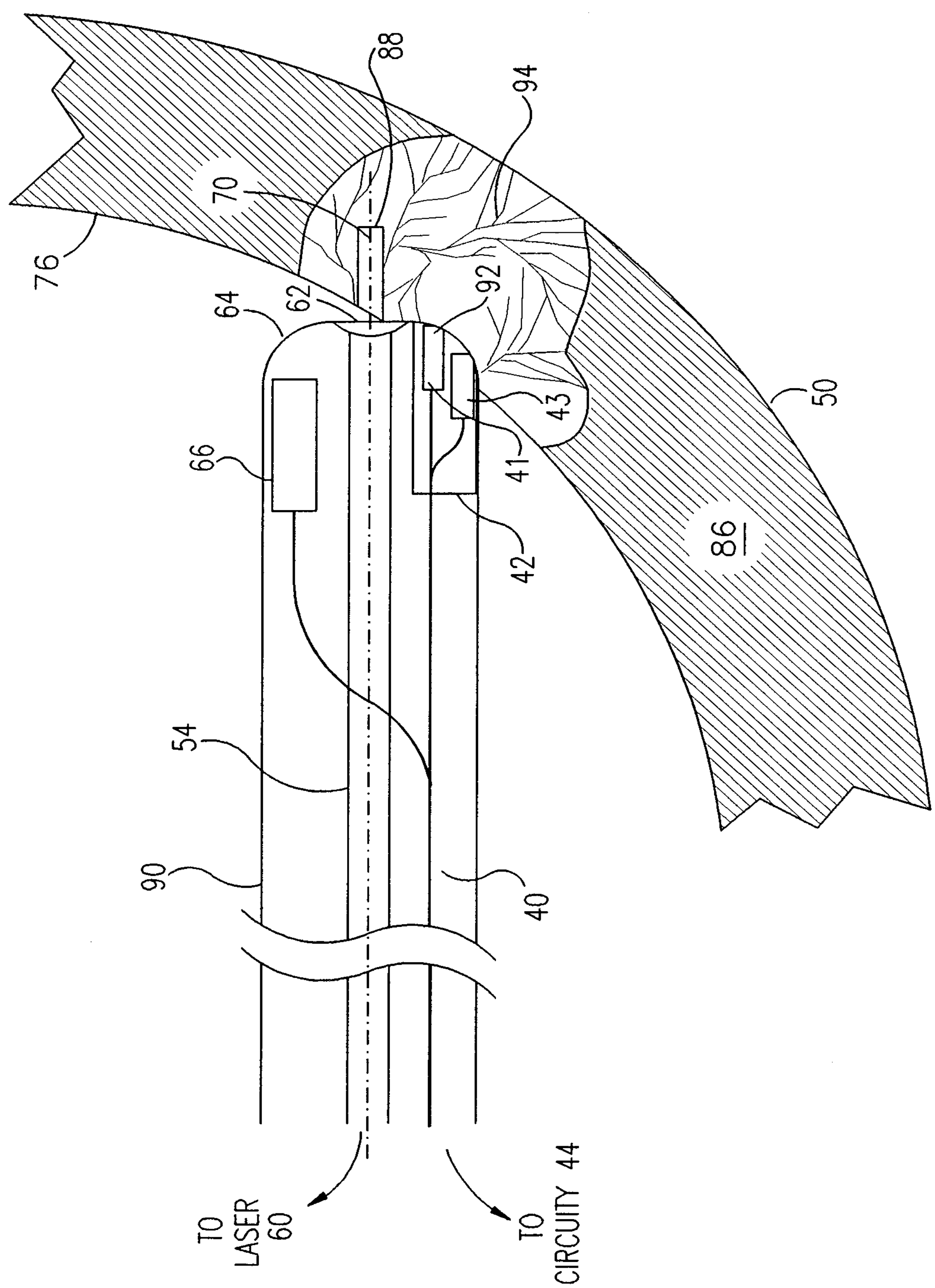
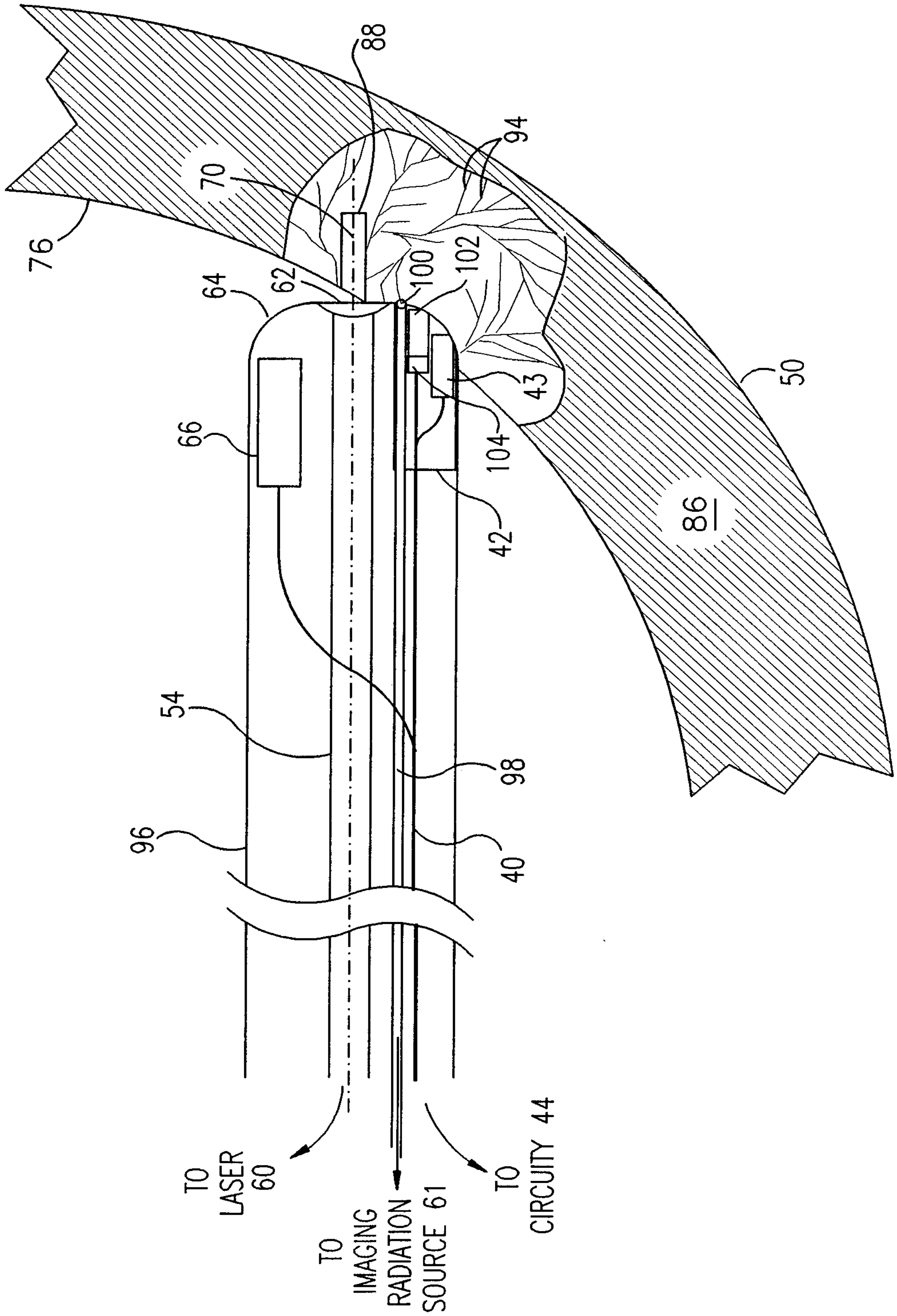

88
94
70
76
64
62
92
43
41
50
66
42
86
54
90
40
TO
LASER
60
TO
CIRCUITY 44

FIG. 7B


88
94
70
76
102
100
64
62
66
43
50
104
86
42
54
98
96
40
TO LASER 60
TO IMAGING RADIATION SOURCE 61
TO CIRCUITY 44

## INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL97/00307

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :A61B 5/04, 17/36; A61F 2/00, 7/00
US CL :600/515, 517; 606/14, 607/98, 100, 101
According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 600/438, 466, 467, 508, 515, 517; 606/2, 3, 7, 11, 12, 14-18; 607/89, 98-102, 122

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| Y | US 5,389,096 A (AITA et al) 14 February 1995, entire document. | 1 19-23, 42-45 |
| Y | US 5,350,375 A (DECKELBAUM et al.) 27 September 1994, entire document. | 1, 2, 6, 10-12, 23-25, 28, 30-32, 34, 38, 39 |
| A,P | US 5,620,439 A (ABELA et al.) 15 April 1997, entire document. | 1, 23 |
| A,T | US 5,607,421 A (JEEVAVANDAM et al) 04 March 1997, entire document. | 1, 23 |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 21 DECEMBER 1997 | 08 JAN 1998 |

| Name and mailing address of the ISA/US | Authorized officer |
|---|---|
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| Facsimile No. (703) 305-3230 | Telephone No. (703) 308-3173 |